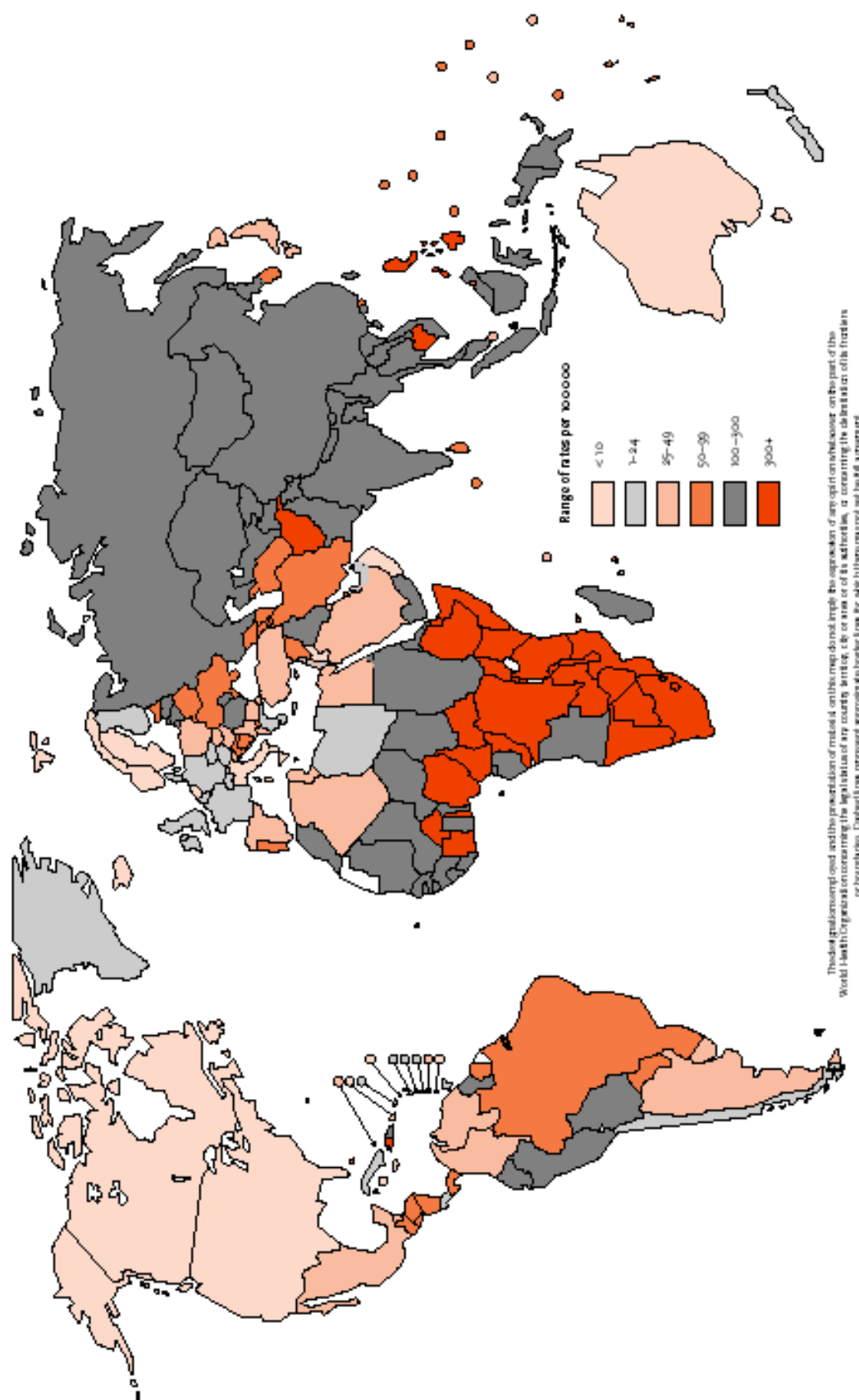


Tuberculosis: A Global Problem

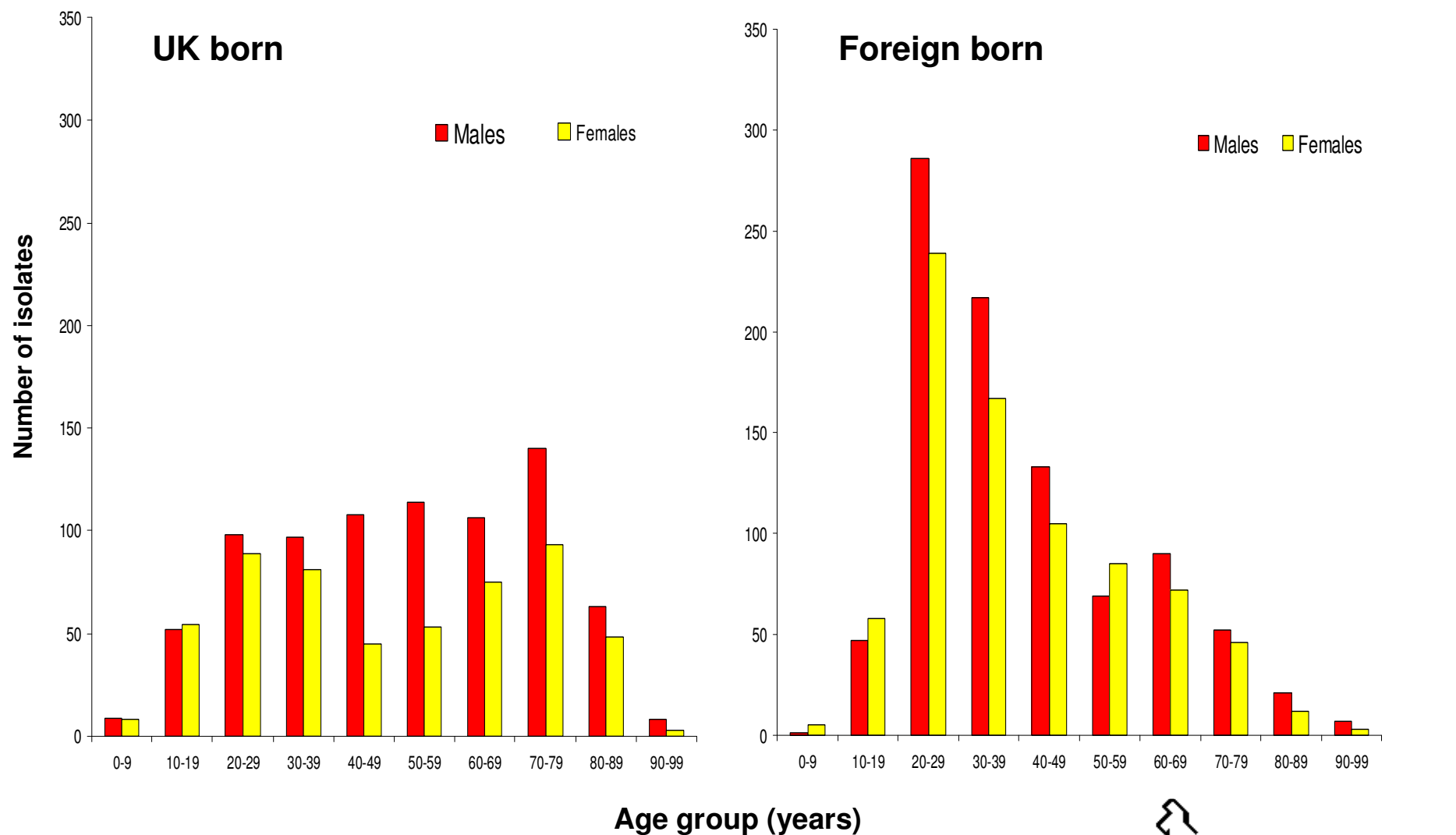
(That does affect Oxford)

1. ESTIMATED TB INCIDENCE RATES, 2000



The data is presented as a world map where each country is shaded according to its TB incidence rate in 2000. The legend indicates six ranges of rates per 100,000 people. High incidence rates (300+ per 100,000, dark red) are prevalent in sub-Saharan Africa, including countries like Nigeria, DRC, and South Africa. Moderate to high rates (100-300, grey) are found in parts of South America (e.g., Brazil) and Eastern Europe. Lower rates (25-49, orange) are seen in Southeast Asia and parts of the Pacific. The lowest rates (<10, light orange) are concentrated in North America, Europe, and Australia. Dashed lines on the map represent approximate borders for which data is not yet finalized.

Numbers of initial isolates of M. tuberculosis complex by age group & sex in UK and foreign born patients, 1999



Source: UK Mycobacterial Resistance Network (Mycobnet) database, April 2001

TB Diagnosis: Issues to Consider

- Diagnosis of latent TB
- Diagnosis of active TB
- Diagnosis in immunocompromised:
 - HIV
 - Drugs
 - Malnutrition
- Finding MDRTB
- Assessing response to therapy
- Assessing relapse / reinfection

Current diagnostic strategies

- Active disease
 - Clinical
 - Radiological
 - Sputum microscopy and culture
 - Histology
 - Response to empiric therapy
- Latent disease
 - Tuberculin skin test (TST)

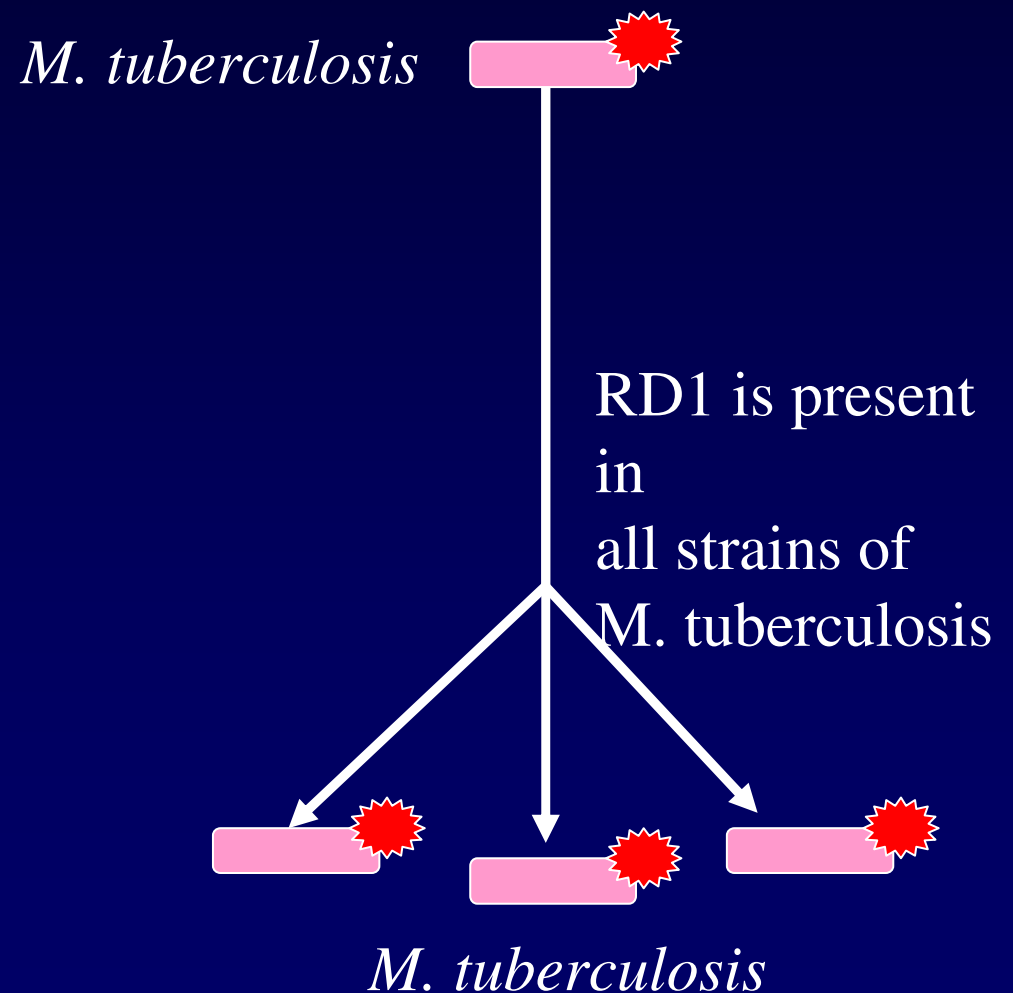
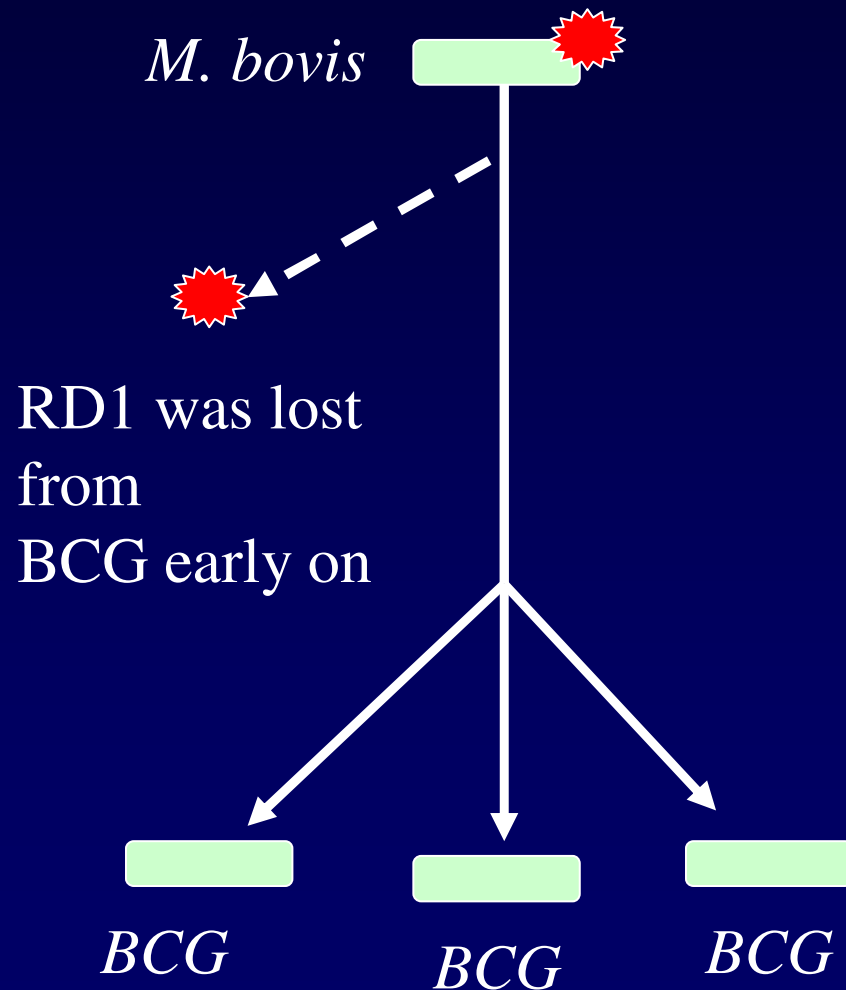
Latent TB

New boy on the block

- IFN - gamma assays
 - Response to PPD as Ag
 - Response to ESAT-6
 - Early secretory antigenic target 6
 - Response to CFP-10
 - Culture filtrate protein-10
- Principle:
 - Infected patient has primed T cells
 - Re-exposure of cells to Ag → activation
 - Activation → IFN- γ secretion

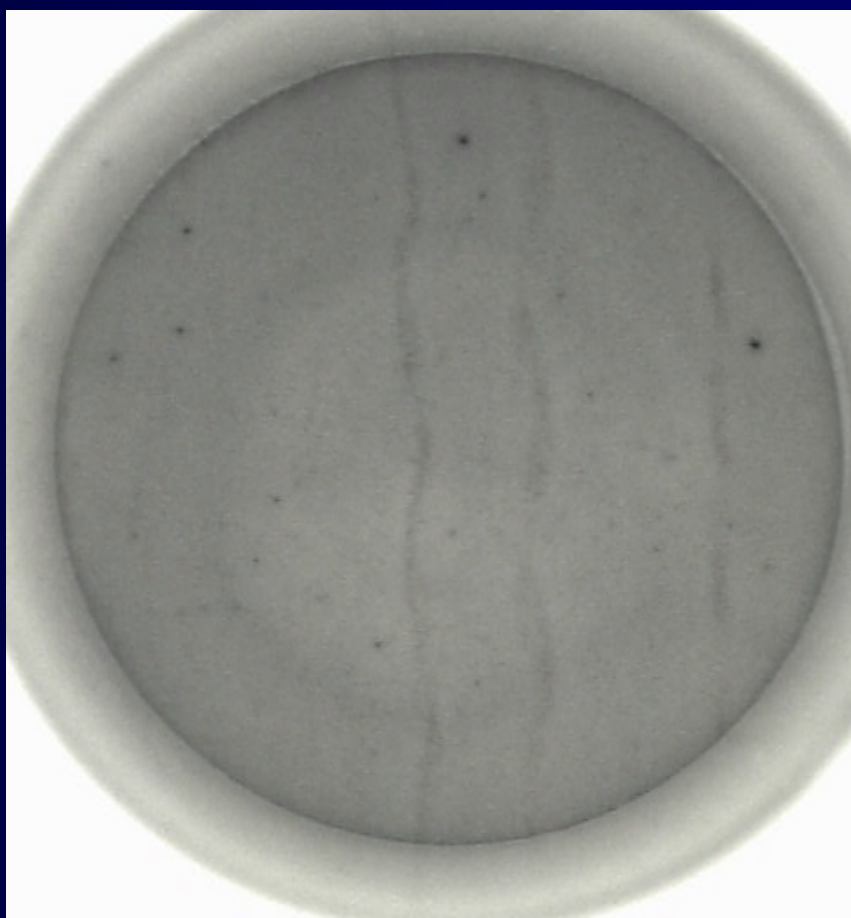
Q: What does *M. tuberculosis* have that BCG doesn't?

☀ RD1 contains the genes for ESAT6 and CFP10



Tests of IFN- γ secretion

- Mantoux / Heaf: recruits T cells to skin
 - PPD as Ag
- Quantiferon – uses PPD as Ag
- Quantiferon-Gold – uses ESAT-6 and CFP-10
 - Measures IFN- γ in supernatant
- T-Spot-TB – uses ESAT-6 and CFP-10
 - Measures IFN- γ by counting activated cells



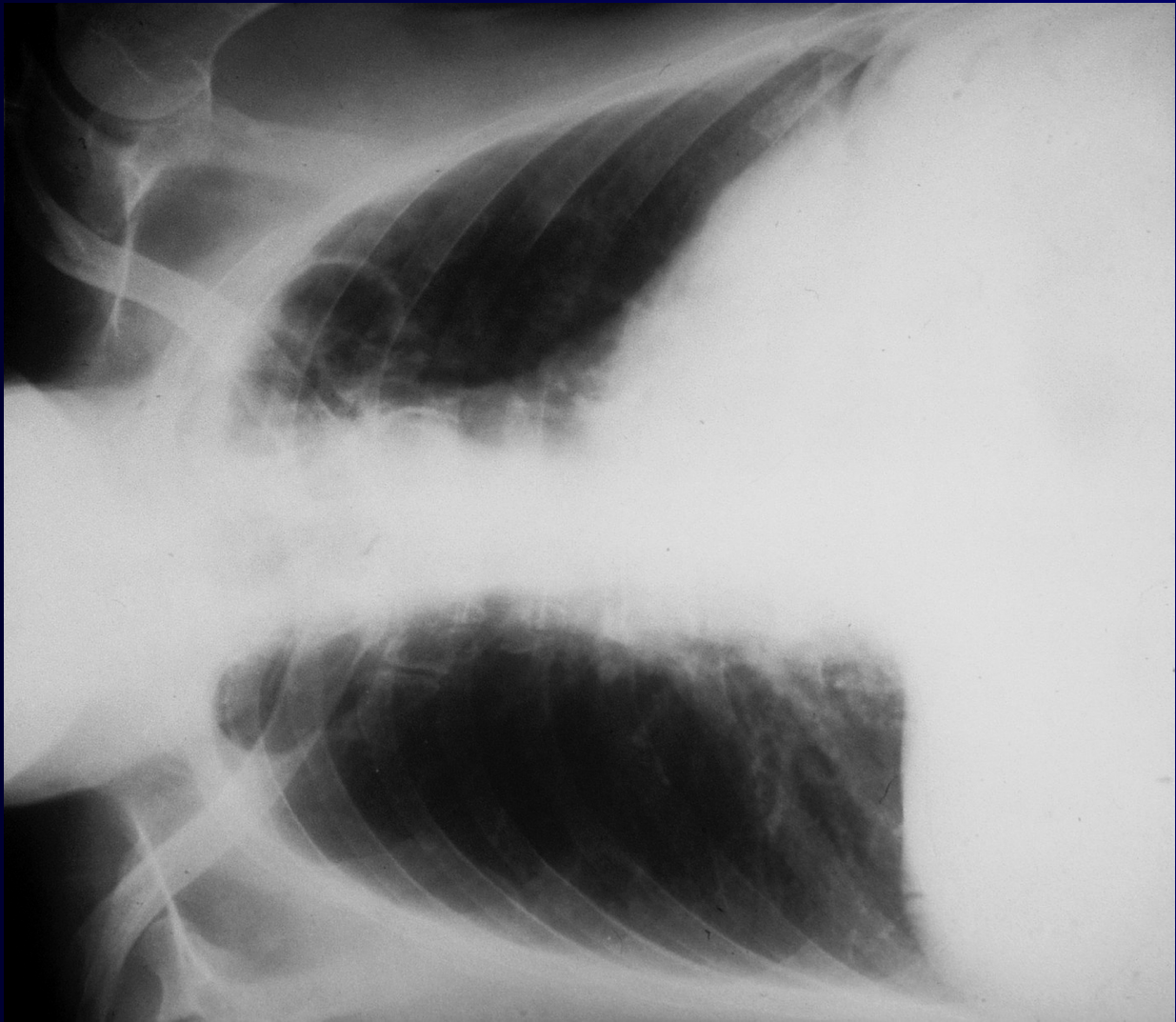
Remaining doubts

- Applicability in highly endemic areas
- Use in immunocompromised
- Screening before, eg., Infliximab
- Use in children
- Atypical infections (*M.kansasii*, *M. marinum*)
- Following treatment
- Considering relapse / reinfection

Conclusions

- Definite advance for latent disease
- Cost remains an issue
 - Only justifiable if large screening programme
- Need prospective cohort of latent infection
- Continued operational research in UK
- Nothing replaces clinical assessment

Active TB



Pulmonary TB

- Most common
- Responsible for most new cases
 - Respiratory transmission
 - $> 10^{12}$ bacilli in a cavity
- Upper lobes predominantly affected
- Cavitation common
 - May be associated with mediastinal LN

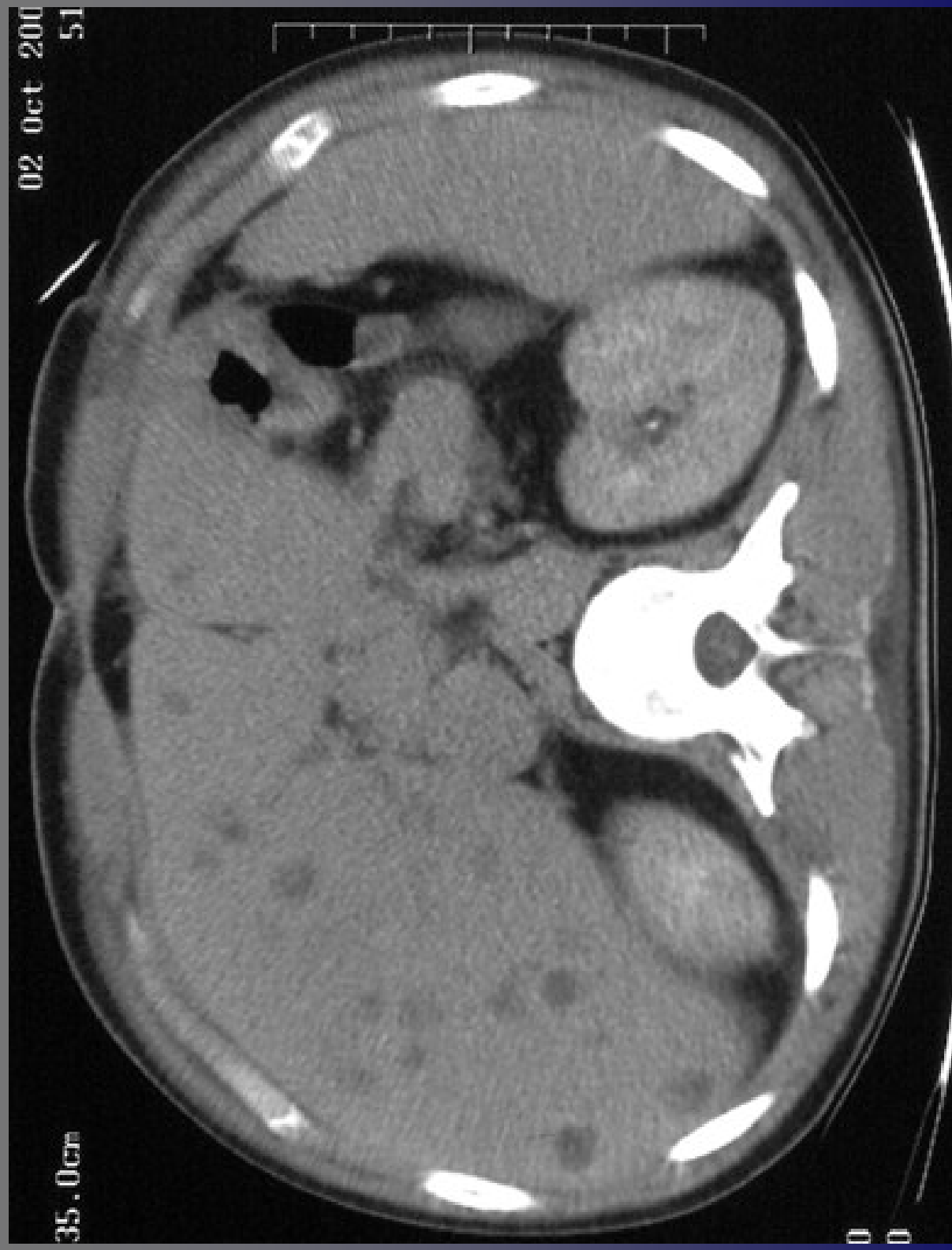
Pulmonary TB

- Diagnosis
 - Clinical history
 - Cough, weight loss, fever, haemoptysis
 - Chest radiograph
 - Sputum
 - Microscopy: positive AFB (ZN or auramine stain)
 - Culture: can take up to 9 weeks
 - Molecular tests: becoming more common



TB lymphadenitis (scrofula)

- Cervical nodes most commonly affected
 - Spread from lungs
 - Haematogenous spread
- Often systemically well
- Chest radiograph often normal
- Biopsy or FNA for diagnosis
 - Not necessary to excise
- 6 months treatment adequate
 - Paradoxical swelling / suppuration occurs



Abdominal TB

3 common presentations

1) ascites

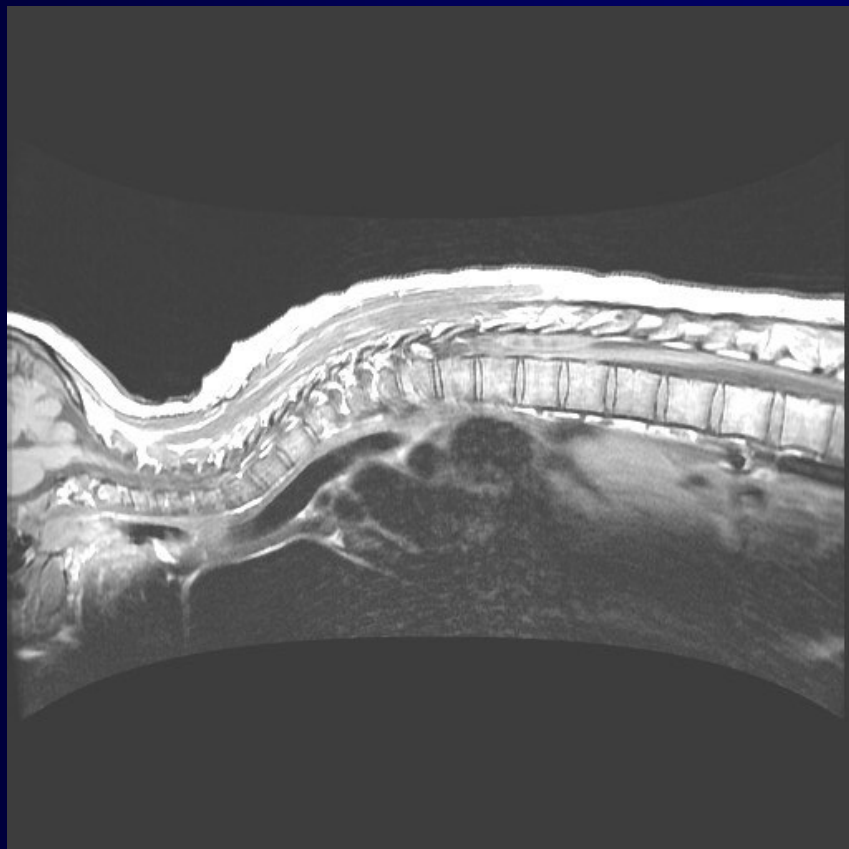
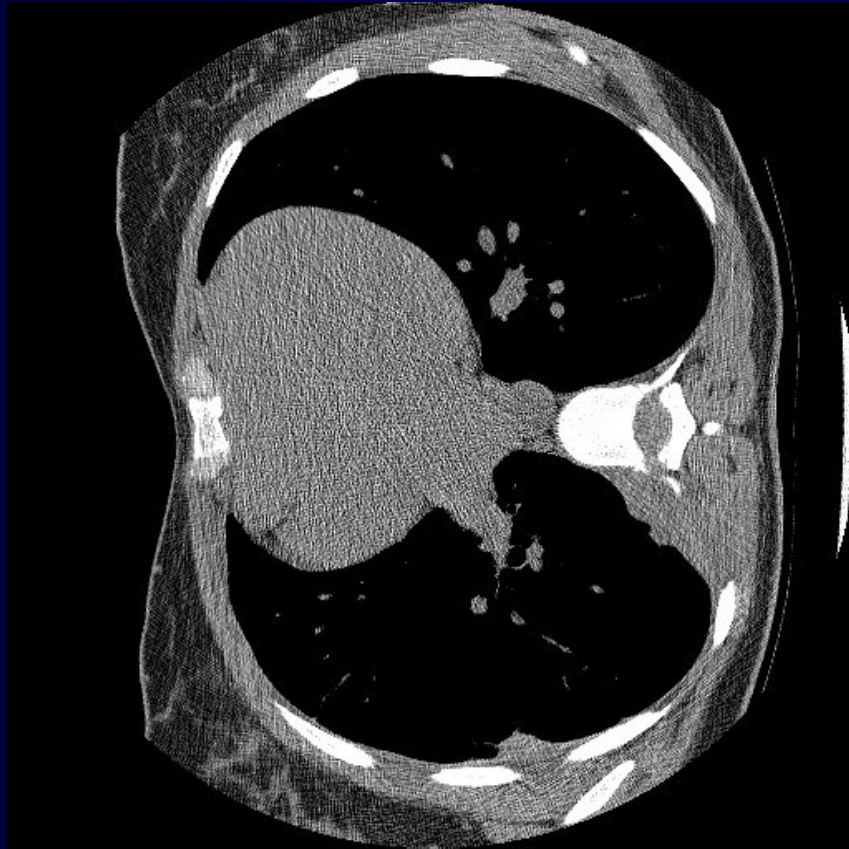
Exudative; rarely AFB seen

2) peritoneal / omental

Doughy abdomen

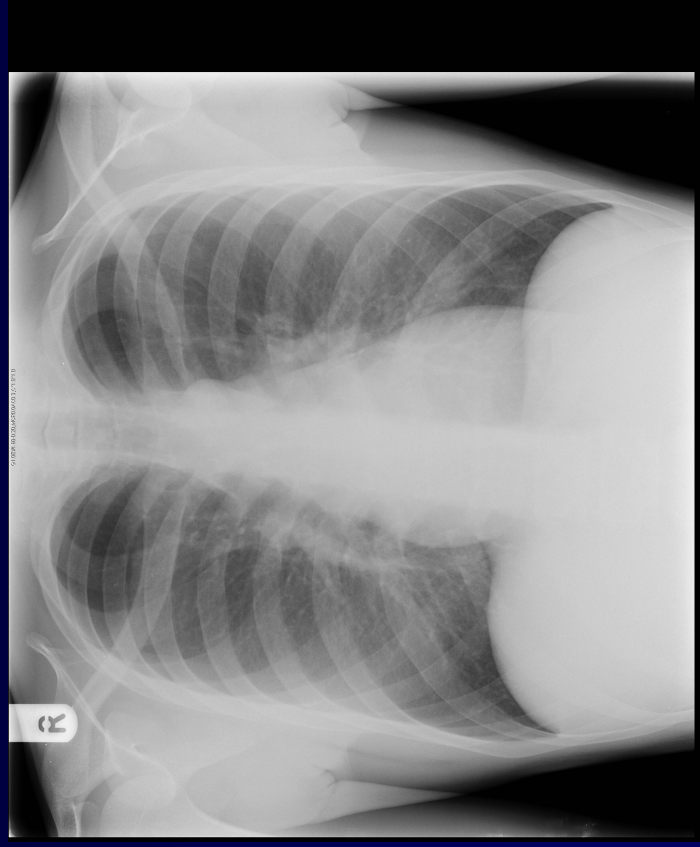
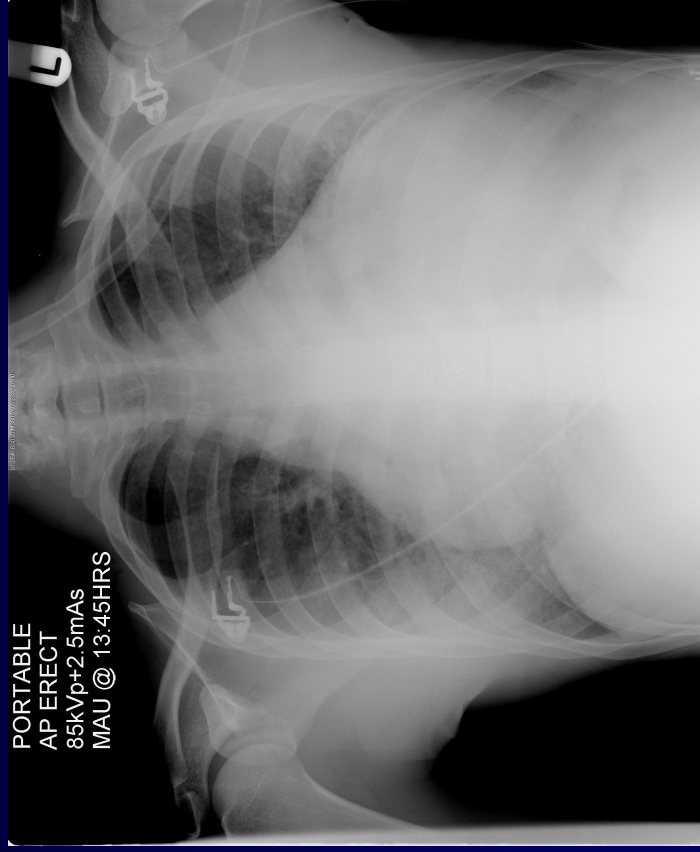
3) intestinal

Bowel symptoms: diarrhoea, obstruction, bleeding



Bone and Joint TB

- Spinal
 - Back pain +/- fever +/- neurology
 - Rarely needs surgery (apart from biopsy)
- TB of long bones
- TB of joints
- May need at least 9 months of therapy



TB pericarditis

- May present with large effusion
- May present with constriction (+/- tamponade)
- Aspirate: effusion; AFB rarely seen
 - Can be blood-stained
- Standard 6 months of treatment
- Steroids for 6 weeks reduces constriction
 - (Strang et al: Lancet 1987; 2: p 1418-1422.)

TB meningitis

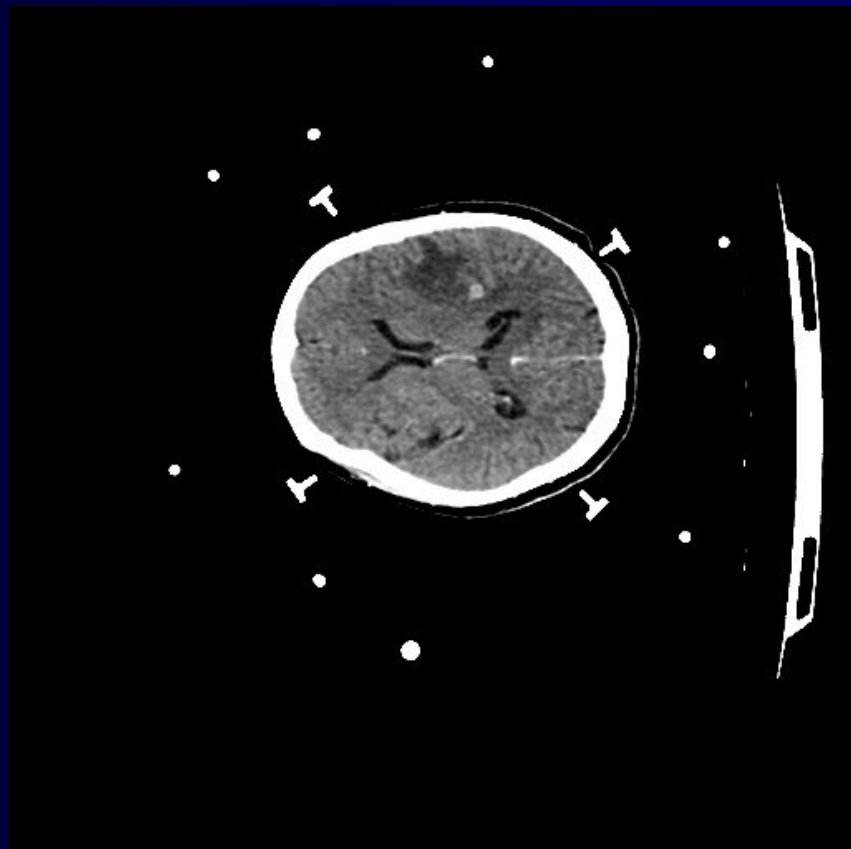
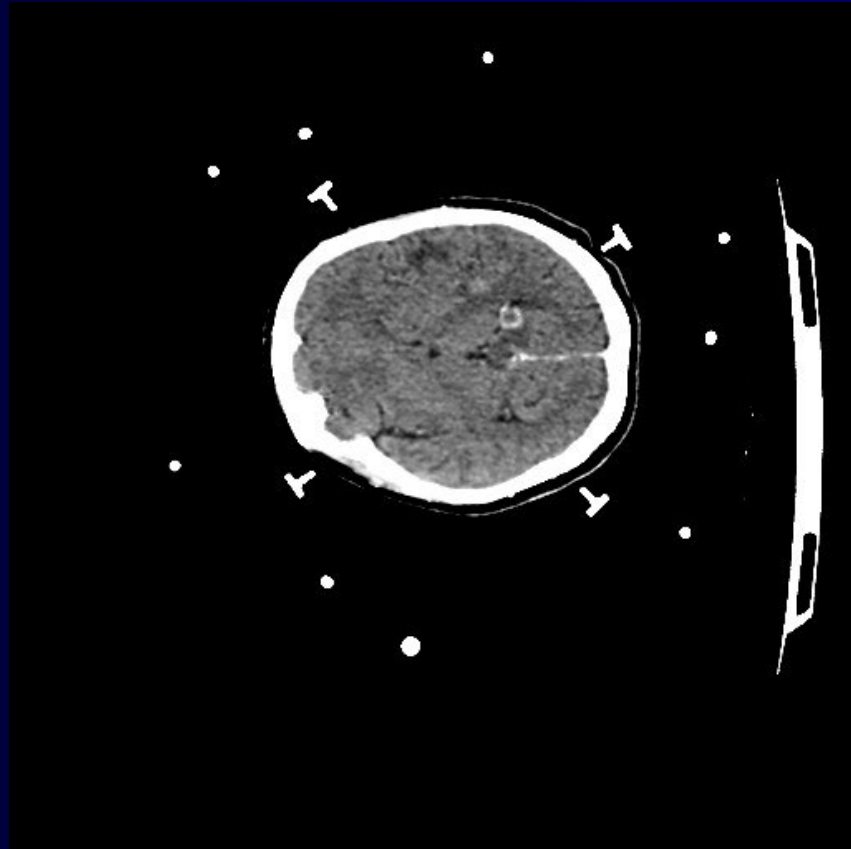
- ‘Chronic’ meningitis (lymphocytic)
- Basal inflammation → vasculitis
 - Cranial nerve palsies: VI > III > others
 - Hydrocephalus
- Variable presentation
 - Headache / neuro signs / coma
- CSF lymphocytic with high protein (may clot)
 - CSF sugar low (< 2/3 plasma level)

TB meningitis - 3

- No trials of length of therapy

Consensus:

- At least 9 months
 - Often go for 12 months
 - INH / PZ good CSF penetration
 - RIF / ETB less good but OK in inflamed meninges
- Dexamethasone beneficial
 - Improved survival (no effect on disability)
 - Thwaites et al NEngJMed 2004; 351: p1741-1751



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